Depression and Antidepressant Medications during Pregnancy

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Nothing to Disclose

EVIDENCE REPORT FOR THE USPSTF

Primary Care Screening for and Treatment of Depression in Pregnant and Postpartum Women

- Pregnant and postpartum women should be screened for depression
- Need “adequate systems” in place for accurate diagnosis, effective treatment and follow-up
- Setting and timing of screening not clear
- Harms of screening “small to none” – insurance?
- EPDS>13 sensitivity 0.80, specificity 0.90

O’Connor E et al., JAMA 2016;315:388-406; Siu AL et al., JAMA 2016;315:380-7.

Edinburgh Postnatal Depression Scale (EPDS)

In the past 7 days:

I have been able to laugh and see the funny side of things:
- 0 As much as I always could
- 1 Not quite so much now
- 2 Definitely not so much now
- 3 Not at all

I have looked forward to enjoyment in things:
- 0 As much as I ever did
- 1 Rather less than I used to
- 2 Definitely less than I used to
- 3 Hardly at all

I have blamed myself unnecessarily when things went wrong:*
- 3 Yes, most of the time
- 2 Yes, some of the time
- 1 Not very often
- 0 No, never

I have felt worried and anxious for no very good reason:
- 0 No, not at all
- 1 Hardly ever
- 2 Yes, sometimes
- 3 Yes, very often

I have felt scared or panicky for no very good reason:*
- 3 Yes, quite a lot
- 2 Yes, sometimes
- 1 No, not much
- 0 No, not at all

Things have been getting on top of me:*
- 3 Yes, most of the time I haven't been able to cope at all
- 2 Yes, sometimes I haven't been coping as well as usual
- 1 No, most of the time I have coped quite well
- 0 No, I have been coping as well as ever

I have been so unhappy that I have had difficulty sleeping:*
- 3 Yes, most of the time
- 2 Yes, sometimes
- 1 Not very often
- 0 No, not at all

I have felt sad or miserable:*
- 3 Yes, most of the time
- 2 Yes, quite often
- 1 Not very often
- 0 No, not at all

I have been so unhappy I have been crying:*
- 3 Yes, most of the time
- 2 Yes, quite often
- 1 Only occasionally
- 0 No, never

The thought of harming myself has occurred to me:*
- 3 Yes, quite often
- 2 Sometimes
- 1 Hardly ever
- 0 Never

Cox JL et al., Br J Psychiatry 1987;150:782-6.

EVIDENCE REPORT FOR THE USPSTF

Primary Care Screening for and Treatment of Depression in Pregnant and Postpartum Women

- Screening pregnant and postpartum women for depression reduces depressive symptoms
- CBT improves outcomes in perinatal women with depression, harms “small to none”
- CBT less studied in pregnancy than postpartum
- Harms to fetus from SSRIs/SNRIs “small to moderate”, likelihood of serious harms “low”

O’Connor E et al., JAMA 2016;315:388-406; Siu AL et al., JAMA 2016;315:380-7.

EVIDENCE REPORT FOR THE USPSTF

Primary Care Screening for and Treatment of Depression in Pregnant and Postpartum Women

“…because these are observational studies, causality cannot be determined; it is not possible to control for all possible confounders related to depression, particularly the fact that women with more severe depression may be more likely to take antidepressants during pregnancy.”

O’Connor E et al., JAMA 2016;315:388-406; Siu AL et al., JAMA 2016;315:380-7.

Depression During Pregnancy

- 7-13% prevalence of depression; 1-6% MDD[1,2]
- Risk factors: previous MDD, adolescence, lower SES, poor social support, anxiety, intimate partner violence, recent negative life event, high preconception BMI, diabetes, obstetric risk[3-5]
- Pregnancy not protective, may be a time of risk
- Possible increased suicidal ideation, decreased completion of suicide[6]

[1]Bennett HA et al., Obstet Gynecol 2004;103:698-709; [2]Gavin NI et al., Obstet Gynecol 2005;106:1071-83, [3]Lancaster CA et al., Am J Obstet Gynecol 2010;202:5-14; [4]Melville JL et al., Obstet Gynecol 2010;116:1064-70; [5]Koleva H et al., Arch Womens Ment Health 2011;14:99-105; [6]Zhong QY et al., Arch Womens Ment Health 2016;19:463-72.

Effects of Untreated Prenatal Depression, Anxiety and Stress

- Poor self-care, nutrition, health behaviors
- Increased alcohol and drug abuse, smoking
- Increased maternal cortisol
- Spontaneous miscarriage, preeclampsia, C-section, placental abruption
- Increased PTB and LBW, lower Apgar scores

Accortt EE et al., Matern Child Health J 2015;19;1306-37; Alder J et al., J Matern Fetal Neonatal Med 2007;20:189-209; Beijers R, et al., Eur Child Adolesc Psychiatry 2014;23:943-56; Hobel CJ et al., Clin Obstet Gynecol 2008;51:333-48; Zhu P et al., Am J Obstet Gynecol 2010;203:34.e1-8; Davalos DB et al., Arch Womens Ment Health 2012;15:1-14.

Exposure to Untreated Prenatal Depression and the Odds Ratio for PTB and LBW: Meta-Analysis

Of the 6,646 titles initially identified, 23 studies met inclusion criteria, all observational, with a total of 25,663 women.

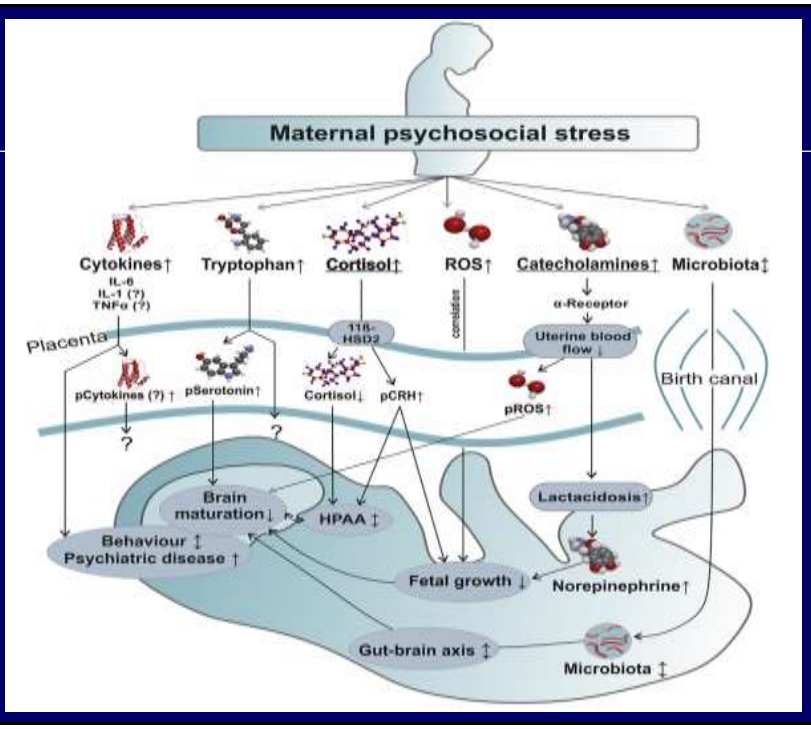
Untreated depression was associated with significantly increased risks of PTB (OR, **1.56**; 95% CI, 1.25-1.94) and LBW (OR, **1.96**; 95% CI, 1.24-3.10), with a trend toward higher risks for exposure to more severe depression.

Jarde A et al., JAMA Psychiatry 2016;73:826-37.

Effects of Untreated Prenatal Depression, Anxiety, and Stress on Child Development

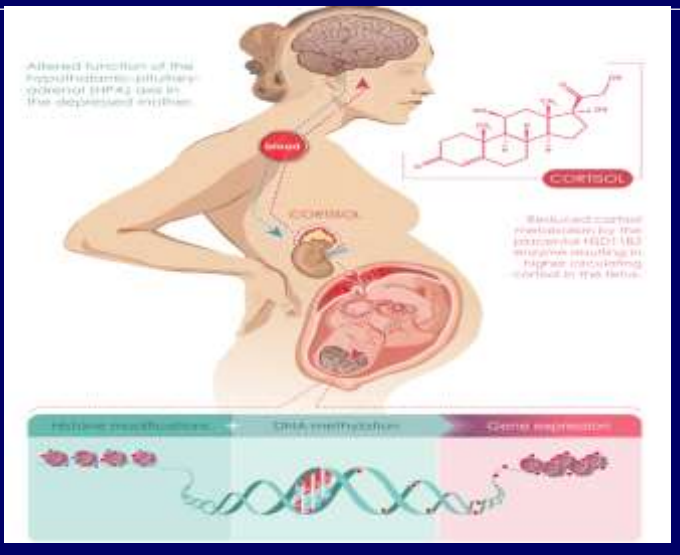
- Altered HPA axis function
- Altered immune function
- Developmental delay, autism
- Cognitive impairment
- Internalizing behaviors
- Externalizing behaviors: ADHD, conduct disorders, antisocial behavior
- Depression, anxiety and psychotic disorders

Beijers R et al., Eur Child Adolesc Psychiatry 2014;23:943-56; Waters CS et al., Eur Child Adolesc Psychiatry 2014;23:957-71; Graignic-Philippe R et al., Neurosci Biobehav Rev 2014;43:137-62; Stein A et al., Lancet 2014;384:1800-19; Goodman SH & Dimidjian S, Can J Psychiatry 2012;57:530-6; Kingsbury M et al., J Am Acad Child Adolesc Psychiatry 2016;55:709-16.



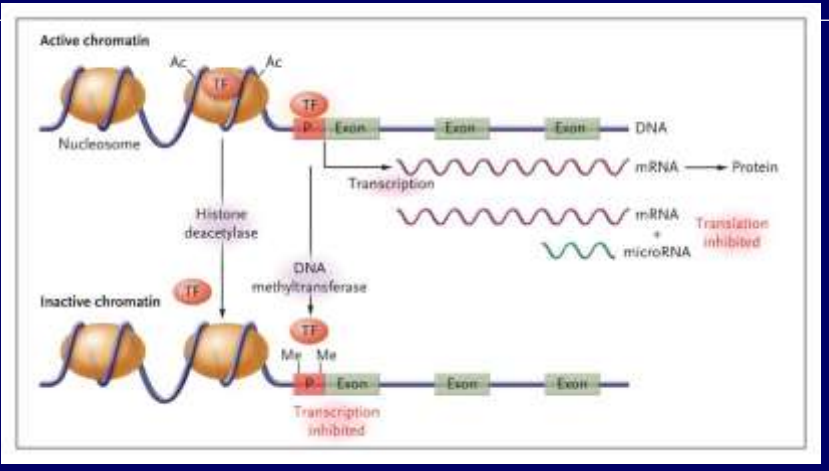
Rakers F et al., Neurosci Biobehav Rev, 2017.

Maternal Depression and Epigenetic Changes



Nemoda Z & Szyf M, Birth Defects Res, 2017;109:888-97.

Regulation of Gene Expression through Epigenetic Processes



Gluckman PD et al., N Engl J Med 2008;359:61-73.

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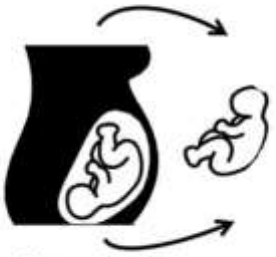
Distress During Pregnancy: Epigenetic Regulation of Placenta Glucocorticoid-Related Genes and Fetal Neurobehavior

- Elevated Perceived Stress Scale scores associated with DNA methylation of 11β-HSD2, NR3C1 and FKBP5 placental glucocorticoid-related genes
- Increased DNA methylation of 11β-HSD2 and NR3C1 associated with decreased fetal coupling (correlation of fetal movement and heart rate which predict more mature neurobehavioral development at birth)

Monk C et al., Am J Psychiatry 2016;173:705-13.

Stress and Infant Neurodevelopment via Maternal Microbiota

Contribution of Maternal Physiology
- Stress response
  - Hypothalamic-Pituitary-Adrenal Axis
  - Inflammatory Changes
- Epigenetic regulation
  - Methylation changes in placenta/cord blood

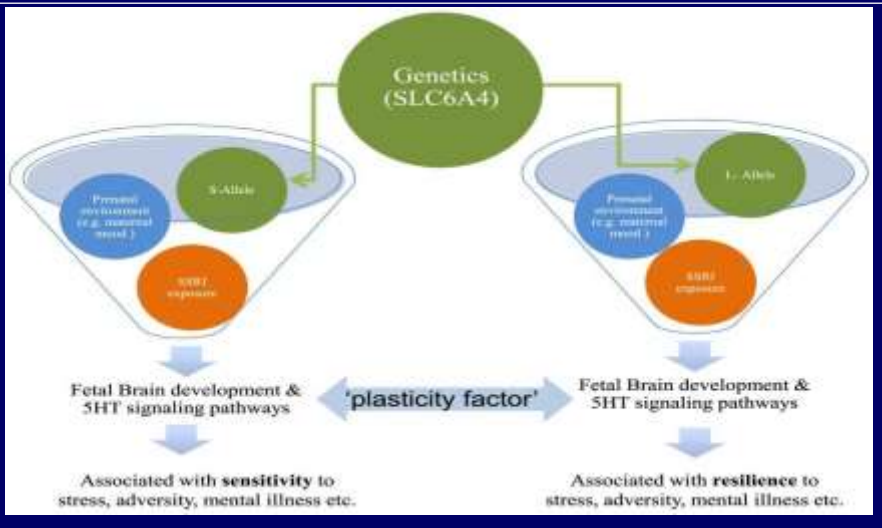


Infant Neurodevelopment
-Infant brain-gut microbiota interactions
-Epigenetic programming

Maternal Dysbiosis
-Microbial Invasion of Amniotic Cavity
-Passage of dysbiotic microbiota to newborn infant

Gur TL et al., Front Psychiatry 2015;Feb 2;6:5.

Serotonin System

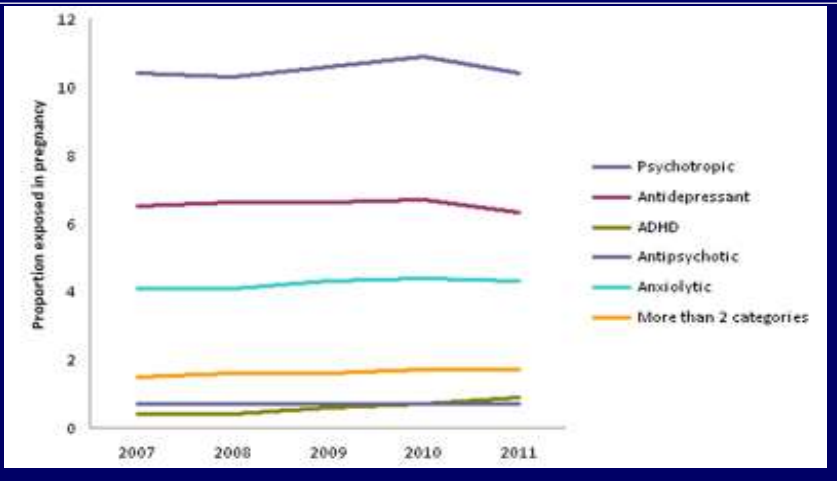


Brummelte S et al., Neuroscience 2017;342:212-31.

Nonpharmacological Treatments

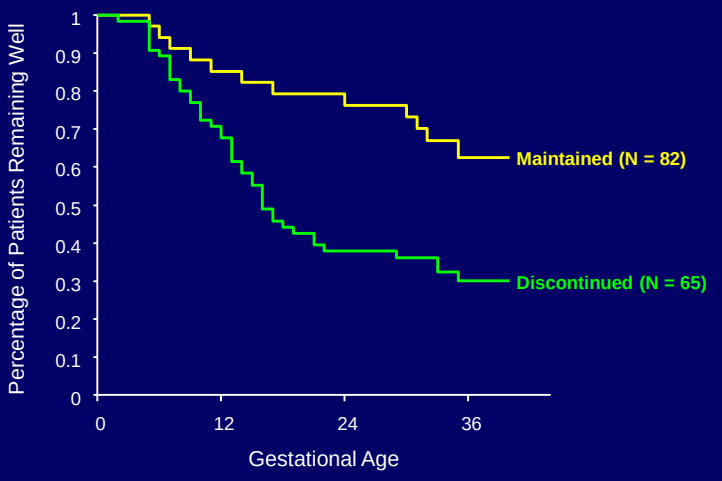
- Psychotherapy: CBT, IPT
- Mindfulness
- Exercise
- Nutritional Supplements e.g. fish oil
- Light Therapy
- Yoga
- Massage
- Acupuncture
- Transcranial Magnetic Stimulation, ECT

Psychotropic Use during Pregnancy



Hanley GE & Mintzes B, BMC Pregnancy Childbirth 2014;14:242.

Time to Relapse in Patients Who Maintained or Discontinued Antidepressant



Cohen LS et al., JAMA 2006:295;499-507.

Previous Medication Classification

A	Controlled studies in pregnancy
B	Human data reassuring and/or animal studies show no risk
C	No human data, animal studies positive or no animal data
D	Human data show risk
X	Human or animal data positive

D: Paroxetine, lithium, valproate, carbamazepine, topiramate

C: Most other psychotropic medications

Pregnancy and Lactation Labeling Rule

SSRIs and Risk of Miscarriage

Table 2. Hazard rates (HRs) of miscarriage in the register population

	First trimester		
	n	*n* cases	HR [95% CI]
Unexposed	1 165 124	108 109	1.00 [Reference]
SSRI exposed	20 612	2105	1.08 [1.04, 1.13]
Discontinued users	5428	613	1.26 [1.16, 1.37]
No use of SSRIs,[a] but diagnosis of depression or anxiety	3417	364	1.00 [Reference]
Use of SSRIs, and diagnosis of depression or anxiety	1633	164	0.96 [0.80, 1.16]
Use of SSRIs, but no diagnosis of depression or anxiety	18 979	1941	0.85 [0.76, 0.95]
No use of SSRIs,[a] and no diagnosis of depression or anxiety	1 167 135	108 358	0.79 [0.71, 0.87]
n	1 191 164	110 827	

[a]Unexposed and discontinued users were categorised as no use of SSRIs.

Johansen RL et al., Paediatr Perinat Epidimiol 2015;29:72-81.

Risk of Spontaneous Abortion after First Trimester Exposure to Antidepressants

TABLE 3. Relative Risk of Miscarriage Among Depressed Women Taking Antidepressants in the First Trimester of Pregnancy Compared With Unexposed Women Without Depression, Uncorrected and Corrected for Induced Abortions

	Total				
	Births + Miscarriage[a]	Births + Miscarriage + ½ Induced Abortions[b]	Miscarriage	Adjusted RR Uncorrected for Induced Abortions (95% CI)	Adjusted RR Corrected for Induced Abortions (95% CI)
Comparison groups					
No medication, no depression	19,335	23,839	1,685	1	1
No medication, depression	7,034	8,877	720	1.1 (1.0, 1.2)	1.1 (1.0, 1.2)
Antidepressant use, depression	1,041	1,498	165	1.5 (1.2, 1.7)	1.3 (1.1, 1.5)
Hypothyroid medication use	697	822	71	1.0 (0.82, 1.3)	1.1 (0.85, 1.3)

Almeida ND et al., Epidemiology 2016;27:538-46.

Meta-Analysis of Antidepressant Exposure vs. No Exposure on Birth Outcomes

- All of the effects from AD exposure were small in magnitude (approximately 3 days shorter gestational age, 75 grams (2.6 ounces) lower birth weight, and less than half a point on the 1 and 5 minute Apgar scores, with values of the exposed group typically falling within the normal range
- Clinical significance of these risks therefore questionable

Ross LE et al., JAMA Psychiatry 2013;70:436-43.

Odds Ratios of Preterm Birth with Antidepressant Use during Pregnancy

- First trimester exposure: 1.16 (0.92-1.45) n.s.
- Exposure at any point: 1.53 (1.40-1.66)
- Third trimester exposure: 1.96 (1.82-2.38)[1]

- Exposure during pregnancy: 1.24 (1.09-1.41)[2]

[1]Huybrechts KF et al., PLoS One 2014;9:e92778; [2]Eke AC et al., BJOG 2016;123:1900-7.

Antidepressant use during pregnancy and the risk of major congenital malformations in a cohort of depressed pregnant women: an updated analysis of the Quebec Pregnancy Cohort

organ-specific defects: paroxetine increased the risk of cardiac defects (aOR 1.45, 95% CI 1.12 to 1.88), and ventricular/atrial septal defects (aOR 1.39, 95% CI 1.00 to 1.93); citalopram increased the risk of musculoskeletal defects (aOR 1.92, 95% CI 1.40 to 2.62), and craniosynostosis (aOR 3.95, 95% CI 2.08 to 7.52); TCA was associated with eye, ear, face and neck defects (aOR 2.45, 95% CI 1.05 to 5.72), and digestive defects (aOR 2.55, 95% CI 1.40 to 4.66); and venlafaxine was associated with respiratory defects (aOR 2.17, 95% CI 1.07 to 4.38).

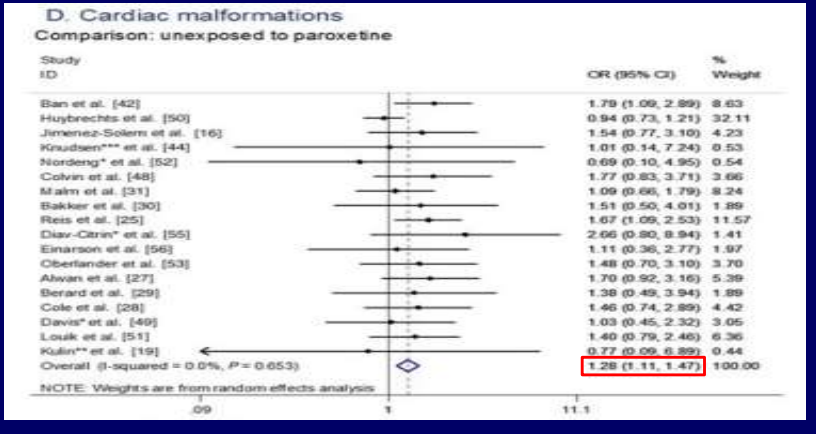
Berard A et al., BMJ Open 2017;7(1):e013372.

Antidepressants and Congenital Malformations

- Very small increase in absolute risk of congenital malformations with first trimester SSRI exposure[1,2]
- Inconsistent defects: septal heart defects, omphalocele, craniosynostosis, anencephaly, ventricular outflow tract heart defects
- Small significant increase in risk of cardiovascular malformations and septal heart defects[3]
- Paroxetine significantly associated with cardiovascular malformations[2-4]

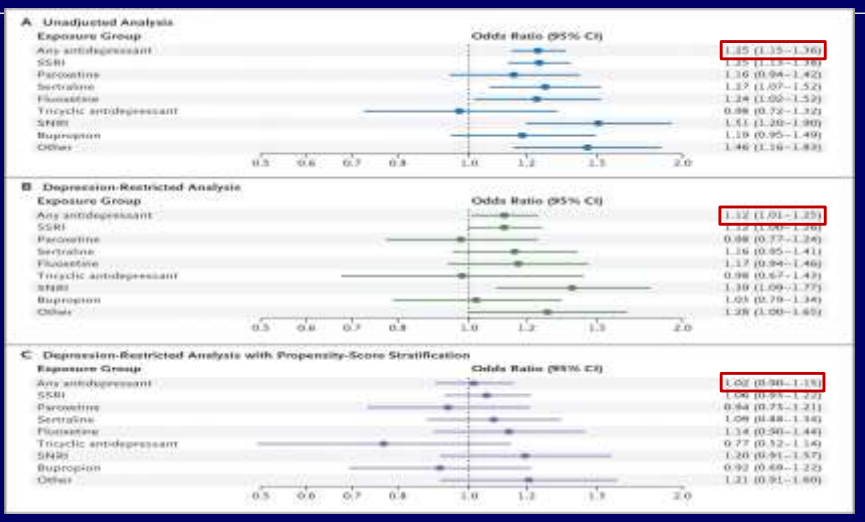
[1]Jordan S et al., PLoS One 2016;11:e0165122; [2]Alwan S et al., CNS Drugs 2016;30:499-515; [3]Grigoriadis S et al., J Clin Psychiatry 2013;74:e293-308; [4]Myles N et al., Aust N Z J Psychiatry 2013;47:1002-12.

Exposure to Paroxetine and Risk of Cardiovascular Malformations



Berard A et al., Br J Clin Pharmacol 2016;81:589-604.

Risk of Cardiac Malformation in Infants According to Maternal Exposure to Antidepressants



Huybrechts KF et al., N Engl J Med 2014;370:2397-407.

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Persistent Pulmonary Hypertension of the Newborn (PPHN)

- Failure of pulmonary vascular resistance to decrease at birth
- Decreased pulmonary blood flow leading to unoxegenated blood to be shunted R to L to systemic circulation
- Hypoxemia, respiratory distress
- 1-2/1,000 live births
- 10-20% mortality

PPHN cont.

- Etiological theories include inhibition of vasodilator nitric oxide, increase in pulmonary smooth muscle proliferation, pulmonary vascular remodeling, genetic polymorphisms[1-4]
- Risk factors include meconium aspiration, cesarean delivery, high BMI, PTD, LGA, diabetes, smoking[4-6]

[1]Chambers CD et al., N Engl J Med 2006;354:579-87; [2]Fornaro E et al., Am J Respir Crit Care Med 2007;176:1035-40; [3]'t Jong G et al., Reprod Toxicol 2012;34:293-7; [4]Occhiogrosso M et al., Am J Psychiatry 2012;169:134-40; [5]Hernandez-Diaz S et al., Pediatrics 2007;120:e272-82; [6]Winovitch KC et al., J Matern Fetal Neonatal Med 2011;24:1398-402.

Risk of PPHN with SSRIs

Meta-analysis: 2.5 higher risk with SSRI exposure in late pregnancy, absolute risk difference 2.9-3.5 per 1,000 infants[1]

- 6.1 higher risk with SSRI exposure after week 20[2]
- 2.3 risk with use in early pregnancy, 2.56 in later pregnancy, 3.44 throughout pregnancy[3]
- 2.1 higher risk with SSRI exposure after week 20[4]
- 4.6 higher risk with SSRI exposure after week 20[5]

[1]Grigoriadis S et al., BMJ 2014;348:f6932; [2]Chambers CD et al., N Engl J Med 2006;354:579-87; [3]Reis M & Kallen B, Psychol Med 2010;40:1723-33; [4]Kieler H et al., BMJ 2012;Jan 12;344:d8012; [5]Berard A et al., Br J Clin Pharmacol 2017;83:1126-33.

Antidepressant Use Late in Pregnancy and Risk of Persistent Pulmonary Hypertension of the Newborn

Krista F. Huybrechts, MS, PhD; Brian T. Bateman, MD, MSc; Kristin Palmsten, ScD; Rishi J. Desai, PhD; Elisabetta Patorno, MD, DrPH; Chandrasekar Gopalakrishnan, MD, MPH; Raisa Levin, MS; Helen Mogun, MS; Sonia Hernandez-Diaz, MD, DrPH

RESULTS A total of 128 950 women (3.4%) filled at least 1 prescription for antidepressants late in pregnancy: 102 179 (2.7%) used an SSRI and 26 771 (0.7%) a non-SSRI. Overall, 7630 infants not exposed to antidepressants were diagnosed with PPHN (20.8; 95% CI, 20.4-21.3 per 10 000 births) compared with 322 infants exposed to SSRIs (31.5; 95% CI, 28.3-35.2 per 10 000 births), and 78 infants exposed to non-SSRIs (29.1; 95% CI, 23.3-36.4 per 10 000 births). Associations between antidepressant use and PPHN were attenuated with increasing levels of confounding adjustment. For SSRIs, odds ratios were 1.51 (95% CI, 1.35-1.69) unadjusted and 1.10 (95% CI, 0.94-1.29) after restricting to women with depression and adjusting for the high-dimensional propensity score. For non-SSRIs, the odds ratios were 1.40 (95% CI, 1.12-1.75) and 1.02 (95% CI, 0.77-1.35), respectively. Upon restriction of the outcome to primary PPHN, the adjusted odds ratio for SSRIs was 1.28 (95% CI, 1.01-1.64) and for non-SSRIs 1.14 (95% CI, 0.74-1.74).

JAMA. 2015;313(21):2142-2151.

Post-Delivery

- Longer term risks associated with untreated antenatal depression
- Longer term risks associated with SSRIs
  - Postnatal adaption
  - Autism

Newborn and Child Outcome Risks Associated with Antenatal Depression & SSRIs

Antenatal Depression

- Impact on newborn
  - Reduced breastfeeding initiation
    - OR=0.68, 95% CI 0.61-0.76

Grigoriadis et al. J Clin Psychiatry. 2013; 74:4:e321-341

Antenatal Depression

- Impact on Child Development
  - Behavioral problems (age 3-7 y/o)
    - Child Behavior Checklist
    - Connors' Parent Rating Scale

Nulman et al; Am J Psychiatry. 2012; 169:1165-1174

Antenatal Depression

- Impact on Child Development
  - Ages 1.5, 3 and 6 years old
    - Child Pervasive Developmental Problems
      - OR=1.44, 95% CI 1.07-1.93
    - Affective Problems
      - OR=1.44, 95% CI 1.15-1.81

El Marroun et. al; Br J Psychiatry. 2014; 205:95-102

Antenatal Depression

- Impact on Child Development
  - Sibling Analysis
  - Behavioral problems (18 and 36 mo)
    - Child Behavior Checklist

Brandlistuen et al; Int J Epidemiol. 2015; 44:1397-1407

Antenatal Depression

- Impact on Adolescents
  - Major Depression
  - RR: 1.28, 95% CI, 1.08-1.51

Pearson et.al. JAMA Psychiatry. 2013; 70(12):1312-1319

Risks of SSRIs on Newborn Outcomes

- Neonatal Adaption Syndrome
- ~ 30% of newborns exposed to SRIs
  - Onset after delivery, peak 2-3 days
  - Symptoms short-term, full recovery by 2 weeks

Chambers et.al. NEJM 1996; 335;1010-1015. Moses-Kolko et.al., JAMA 2005; 293:2372-2383. Laine et. al. Arch Gen Psych 2003; 60:720-726

Risks of SSRIs on Newborn Outcomes

- Symptoms NAS
  - Irritability, tremors, jitteriness, muscle tone
  - Trouble feeding, agitation, respiratory distress and poor sleep
  - Less common: abnormal posturing and shivering
  - Rare: seizure

Chambers et.al.NEJM 1996; 335;1010-1015. Moses-Kolko et.al. JAMA 2005; 293:2372-2383. Laine et.al. Arch Gen Psych 2003; 60:720-726

The Roles of Maternal Depression, Serotonin Reuptake Inhibitor Treatment, and Concomitant Benzodiazepine Use on Infant Neurobehavioral Functioning Over the First Postnatal Month

Amy L. Salisbury, Ph.D., Kevin E. O'Grady, Ph.D., Cynthia L. Battle, Ph.D., Katherine L. Wisner, M.D., M.S., George M. Anderson, Ph.D., Laura R. Stroud, Ph.D., Cynthia L. Miller-Loncar, Ph.D., Marion E. Young, Ph.D., Barry M. Lester, Ph.D.

- Neurobehavior over 1st month of life
  - 1) Untreated Depression
  - 2) Prenatal SSRI Exposure
  - 3) Prenatal SSRI & Benzo Exposure
  - 4) No depression, no SSRI or Benzo

Salisbury et.al. Am J Psychiatry. 2016; 173:2:147-156

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- No group differences
  - Birth Weight, Gestational Age, APGAR Scores, NICU Admissions, Respiratory Distress or Breastfeeding

Salisbury et.al. Am J Psychiatry. 2016; 173:2:147-156

The Roles of Maternal Depression, Serotonin Reuptake Inhibitor Treatment, and Concomitant Benzodiazepine Use on Infant Neurobehavioral Functioning Over the First Postnatal Month

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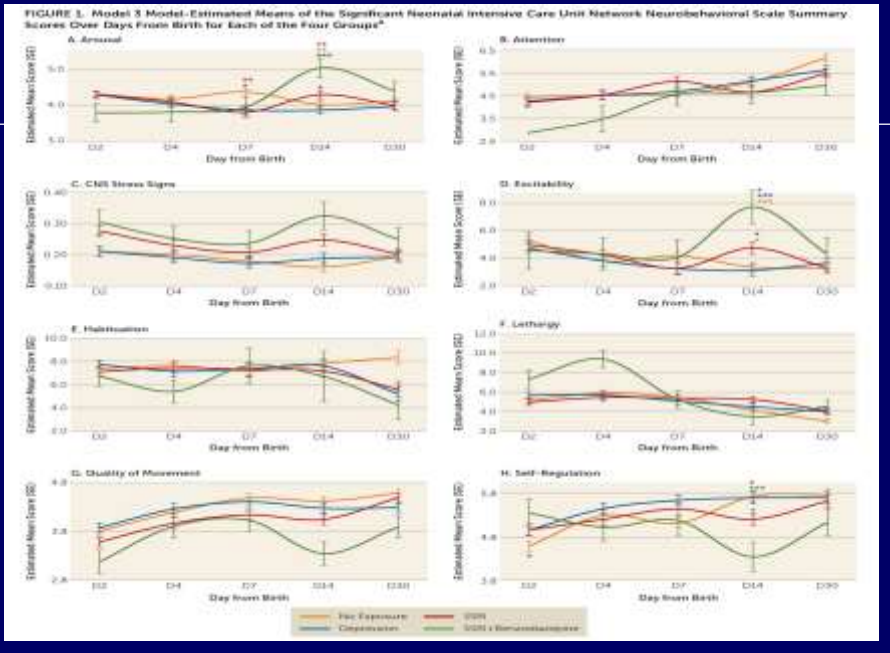
- 5/13 neonatal symptoms reach statistical significance, but when controlling for depression only 2 sx
  - SSRI and SSRI plus benzo groups
    - Lower quality of movement and higher levels of CNS depressive symptoms, compared to depression only or no exposure groups

Salisbury et.al. Am J Psychiatry. 2016; 173:2:147-156



Salisbury et.al. Am J Psychiatry. 2016; 173:2:147-156

Risks of SSRIs on Newborn Outcomes

- Secondary Analysis
  - No difference in neurobehavioral scores in women who d/c SSRI in last month of pregnancy vs. continued SSRI throughout

Salisbury et.al. Am J Psychiatry. 2016; 173:2:147-156

Risks of SSRIs & Autism Spectrum Disorder (ASD)

Are Antidepressants Safe During Pregnancy?

New Research Raises More Questions about Antidepressant Use During Pregnancy

Risks of SSRIs & ASD

- 2017, 6 Meta-Analyses
  - Kobayashi et al., Reprod Toxicol 2016;65:170-178
  - Kaplan et al., Reprod Toxicol 2016; 66:31-43
  - Brown et al., J Clin Psych 2017;78(1)e48-e58
  - Mezzacappa et al. JAMA Ped. 2017;17(6):555-563
  - Kaplan et al., Br J Clin Pharm 2017 epub
  - Andalib et al., Eur Psychiatry 2017. pub online

Andrade. 2017 J Clin Psychiatry; 138: e1-:e5

Risks of SSRIs & ASD

- Summary of 6 Meta-Analyses
  - All Agree: Perinatal SSRI exposure is a MARKER for increased risk for ASD in offspring
  - 5/6 Agree: SSRI and ASD Association
    - Decreased in magnitude and significance when accounted for confounding variables
    - Mostly non-significant when there was control for maternal psychiatric illness

Andrade. 2017 J Clin Psychiatry; 138: e1-:e5

Risks of SSRIs & ASD

- 2017, 6 Meta-Analyses
  - Kobayashi et al., Reprod Toxicol 2016;65:170-178
  - Case-Control & Cohort Studies
    - Restricted dataset to only mothers with psychiatric illness and found no association between perinatal SSRIs and ASD

Andrade. 2017 J Clin Psychiatry; 138: e1-:e5

Risks of SSRIs & ASD

- 2017, 6 Meta-Analyses
  - Brown et al., J Clin Psych 2017;78(1)e48-e58
  - Restricted analyses to datasets that had controlled for maternal psychiatric illness, and found no association between perinatal SSRIs and ASP

Andrade. 2017 J Clin Psychiatry; 138: e1-:e5

Risks of SSRIs & ASD

- 2017, 6 Meta-Analyses
  - Mezzacappa et al. JAMA Ped. 2017;17(6):555-563
  - Antidepressant exposure prior to conception was associated with increased risk of ASD before and after adjusting for past maternal depression
  - OR=1.77; 95% CI, 1.49-2.09

Andrade. 2017 J Clin Psychiatry; 138: e1-:e5

Risks of SSRIs & ASD

- 2017, 6 Meta-Analyses
  - Kaplan et al., Br J Clin Pharm 2017 epub
  - Maternal psychiatric disorder with no SSRI exposure during pregnancy was associated with an increased risk of ASD
  - OR=1.81; 95% CI, 1.44-2.29

Andrade. 2017 J Clin Psychiatry; 138: e1-:e5

Risks of SSRIs & ASD

- 2017, 6 Meta-Analyses
  - Kaplan et al., Reprod Toxicol 2016; 66:31-43
  - Exclusive preconception exposure to SSRIs was associated with increased risk of ASD
    - OR=1.84, 95% CI: 1.48-2.28

Andrade. 2017 J Clin Psychiatry; 138: e1-:e5

Risks of SSRIs & ASD

- 2017, 6 Meta-Analyses
  - Andalib et al., Eur Psychiatry 2017. pub online
  - No rational for why they excluded studies
  - Overall crude association between perinatal SSRIs and ASD (no adjustments for confounding variables).
    - OR=1.83, 95% CI, 1.59-2.10
  - 3 studies made up 75% of weightage in analysis

Andrade. 2017 J Clin Psychiatry; 138: e1-:e5

Discussion about Risks in Pregnancy

- Established short-term and long-term negative consequences of untreated prenatal depression, anxiety and stress

- First trimester SSRI use: Possible small increased risk of spontaneous miscarriage, PTB and cardiovascular anomalies
- Second trimester use: Increased risk of PPHN after week 20
- Third trimester use: Increased risk of PTB, transient neonatal symptoms esp. respiratory distress
- Potential: HTN, preeclampsia, postpartum hemorrhage

Discussion about Risks in Pregnancy

- Child development with prenatal SSRI use: delayed motor development and control, resolves with age

- Most SSRI risks confounded by underlying disease
- Maximize non-pharmacological treatments
- Maintaining antidepressant not always protective
- Antidepressant dose may need to be increased
- Partially effective prenatal treatment with antidepressants is double exposure

Antidepressant Use and Pregnancy

- Consider taper and discontinuation of antidepressant in women with mild or no symptoms (in remission)
- Consider psychotherapy and complementary/alternative therapies with mild-moderate depression
- Consider continuation of antidepressant in women with current or prior moderate-severe depression
- Carefully document risk benefit discussion about medications, non-pharmacological and complementary/alternative treatments

Susser LC et al., Am J Obstet Gynecol 2016;215:722-30; Yonkers KA et al., Annu Rev Clin Psychol 2014;10:369-92; Alwan S et al., CNS Drugs 2016;30:499-515; Muzik M & Hamilton SE, Matern Child Health J 2016;20:2268-79.

Useful Websites

- www.mothertobaby.org or www.teratology.org
- www.womensmentalhealth.org
- www.motherisk.org
- www.seleni.org
- www.postpartum.net
- www.mcpapformoms.org
- LactMed on toxnet.nlm.nih.gov
- Pregnancy and Lactation Labeling on www.fda.gov